

REMARKS AND ELECTION RESTRICTION

Claims 1-23 were filed in the original case. In accordance with a telephone conversation with the Examiner on April 19, 2002, a provisional election without traverse to prosecute the invention of Group I, claims 1-15 is herein affirmed. Claims 16-23 are withdrawn from further consideration by the Examiner, 37 CAR 1.142(b) as being drawn to a non-elected invention.

Claims 1-23 are hereby cancelled in the present amendment. These cancellations are made without acquiescing to the Examiner's rejections, but are made to further prosecution and Applicant's business interests. The Applicants reserve the right to prosecute Claims 1-23 (or similar claims) in the future. Claims 24-61 are added with the present amendment and are the subject matter of Group I. Therefore, Claims 24-61 are currently pending.

In the Office Action dated February 4, 2003, the Examiner has made a number of rejections. The currently pending rejections are:

- 1) Claims 1-6 and 11-13 are rejected under 35 U.S.C. 102(b); and
- 2) Claims 1-3, 6-9, 11-13 and 15 are rejected under 35 U.S.C. 102(e); and
- 3) Claims 1-6 and 10-14 are rejected under 35 U.S.C. 102b; and
- 4) Claims 1-3, and 6-15 are rejected under 35 U.S.C. 103(a).

Claims 1-23 are cancelled herein, rendering these rejections moot. The Applicants believe that the pending claims are not taught by the prior art and are not obvious. Therefore, Claims 24-61 should be passed into allowance.

Applicants also submit a supplemental information disclosure statement with the present response and amendment. The supplemental information disclosure statement contains copies of references that were identified in the previous information disclosure statement (but where Applicants had not yet obtained copies) and also contains several references cited in a related patent application 09/995,901 (now abandoned).

REJECTIONS

For clarity, the rejections at issue are set forth by number in the order they are herein addressed and are addressed with in view of the new claims.

I. THE CLAIMS ARE NOT ANTICIPATED

The Examiner has rejected the claims as allegedly being anticipated by several references. The Federal Circuit has stated the relevant analysis for anticipation as follows:

"A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."¹

The prior art cited by the Examiner consists of Berger et al., Biochemistry, (1979), Vol 18 (23), pages 5143-5149 (hereinafter "Berger et al"). The Examiner argues "Berger et al inherently teach a method for reducing the activity of an RNase, wherein the activity of the RNase is diminished at least 25-90% relative to the activity of the RNase in the absence of the RNA polymer (Figure 1 and Table 1). Berger et al teach a method, wherein the RNA polymers are selected from poly A (page 5149, column 1, last sentence of first paragraph. Berger et al teach a method, wherein the preparation further comprises a ribonuclease inhibitor (Materials and Methods Section). Berger et al teach a method for reducing the activity of an RNase from a tumor cell (Page 5148, Column 2, Discussion Section)." (Office Action 2/4/03, page 4).

Applicants note that the present claims have split the previous claims (which were generic as to heteropolymers and homopolymers) into a first set of claims (24-43) that comprise heteropolymers and a second set of claims (44-61) that comprise homopolymers.

It is first noted that the cited prior art (Berger et al.) does not teach the double-stranded (polyA:polyU, polyC:polyG) or single-stranded (poly(GU), poly(CU), poly(GI) and poly(CI)) RNA heteropolymers of claims 24-43. Moreover, as the Examiner concedes (Office Action 1/4/2003, page 7), "Berger et al do not teach the method wherein RNase comprises RNase A, RNase B or angiogenin." Therefore Berger et al. fails the each and every element test as set forth by the CAFC.

¹ *Verdegaal Bros. V. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987)

Berger et al. also does not teach all of the elements of claims 44-61. In particular, Berger et al. does not teach the use of isolated, unmodified RNA homopolymers for reducing the activity of an RNase (the specification of the present application explains, for example, at page 21, that “the present invention provides the advantage of using readily available unmodified RNA polymers, rather than the complex and expensive modified polymers”). Berger et al. only describes the use of vanadyl complexed ribonucleoside 5'-monophosphates, but not isolated, unmodified RNA homopolymers. For example, in reference to Figure 1, Berger et al. states “As illustrated in figure 1, most potential nuclease inhibitors were incapable of preventing the degradation of RNA despite their ability to retard nuclease action. Only the equimolar mixture of the four ribonucleoside-vanadyl complexes at 10mM protected the exogenous hnRNA substrate.” Thus, Berger et al. does not teach the presently claimed invention.

The prior art cited by the Examiner also consists of Akitaya et al. (U.S. Patent 6,300,058B1) (October 9, 2001) (hereinafter “Akitaya et al.”). The Examiner argues that “Akitaya et al inherently teach a method, wherein the RNA polymers are selected from poly A or poly C or poly G (Column 8, line 50 to column 9, line 1). This inherence is deduced from the fact the Vanadyl ribonucleoside complex, the inhibitor of RNase is prepared by mixing all four different ribonucleosides in equimolar amount. Akitaya et al teach a method. Wherein the RNA polymers are affixed to a solid support, which is resin or plastic surface (Column 10, line 33 to column 11, line 62). Akitaya et al teach a method, wherein the preparation further comprises a ribonuclease inhibitor RNASIN (Columns 9, lines 1-47). Akitaya et al teach a method for reducing the activity of an RNase from a tumor cell (Example 2).” (Office Action 2/4/2003, pages 5-6).

Akitaya et al. suffers from the same limitations as Berger et al. In particular, Akitaya et al. does not teach or suggest the use of RNA heteropolymers. Likewise, Akitaya et al. is limited to the use of vanadyl ribonucleoside complexes. Thus, Akitaya fails to teach all of the elements and the present invention and does not anticipate the present claims.

Applicants further submit that the cited references do not each all of the elements of each and every dependent claim. The cited references, in addition to not teaching the recited polymers, do not teach or suggest that, for example, the recited polymers

diminish the activity of RNase at least 90% relative to the activity of the RNase in the absence of the RNA polymer (e.g., claim 48) or that, for example, homopolymers comprising polyG have inhibitory properties (e.g., claim 51).

Applicants respectfully submit that neither of the references cited by the Examiner (i.e. Berger et al. or Akitaya et al.) teach each and every element of the Claims as required, and requests that the rejection under 35 USC §102b be withdrawn

II. THE CLAIMS ARE NOT OBVIOUS

The Examiner has rejected claims 1-15 as allegedly being obvious in view of Berger et al. in view of Chatterjee et al. (U.S. Patent 5,965,399) (issued October 12, 1999) (hereinafter “Chatterjee et al.”), and Akitaya et al. in view of Chatterjee et al. None of these references alone, or in combination, teach or suggest compositions and methods for using the single-stranded or double-stranded RNA heteropolymers or isolated, unmodified homopolymers of the present Claims to inhibit RNase enzymes.

The Examiner argues “It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method, wherein RNase comprises RNase A, B or angiogenin of Chatterjee et al. in the the method of Berger et al. since Chatterjee et al. state, “RI is useful in a variety of molecular biology applications where RNase contamination is a potential problem (Column 1, lines 39-41)”. (Office Action 2/4/2003, page 7). The Examiner also argues “It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method, wherein RNase comprises RNase A, B or angiogenin of Chatterjee et al. in the the method of Akitaya et al. since Chatterjee et al. state, “RI is useful in a variety of molecular biology applications where RNase contamination is a potential problem (Column 1, lines 39-41)”. (Office Action 2/4/2003, page 8).

The Applicants assert that the Examiner has not met the burden of establishing a *prima facie* case of obviousness. A *prima facie* case of obviousness requires the Examiner to cite to references that (a) disclose all the elements of the claimed invention, (b) suggest or motivate one of ordinary skill in the art to combine or modify those elements to yield the claimed combination, and (c) provide a reasonable expectation of

success should the combination cited by the Examiner be carried out.² Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicant to allowance of the claims at issue. At a minimum, the Examiner fails to establish a *prima facie* obviousness 1) because the cited references fail to disclose all elements of the claimed invention, 2) and because there is no teaching, suggestion or motivation to make the Examiner's selections and combinations of the cited references. The Applicants assert that the Examiner has failed to establish the requirements for a *prima facie* case of obviousness, thus entitling Applicants to withdrawal of this rejection.

A. The Examiner's cited references fail to disclose all elements of the claimed invention

The RNase inhibitors taught by Berger et al. and Akitaya et al., as described above, do not teach or suggest the heteropolymers or isolated, unmodified homopolymers of the presently claimed invention. Chatterjee et al. does nothing to remedy these deficiencies. Hence, the Examiner's cited references fail to disclose all elements of the presently claimed invention.

B. The Examiner's cited references fail to provide a motivation to combine the the recited elements

An essential requirement for a *prima facie* case of obviousness is whether a person skilled in the art would be motivated to modify the reference to arrive at the claimed invention.³ The requirement that the Examiner make a showing of a suggestion, teaching or

² See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

³ *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988); *In re Jones*, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992)

⁴*In re Sang Su Lee* 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002). See also, *Brown & Williamson Tobacco corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential evidentiary component of an obviousness holding'" (quoting *C.R. Bar, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998))); *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.")

motivation to combine the prior art references is an essential evidentiary component of an obviousness holding. The factual inquiry whether to combine references "must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with."⁴ The law requires that evidence of a suggestion, teaching, or motivation to combine prior art references "must be clear and particular".⁵ "Broad conclusory statements regarding the teaching of multiple references, standing alone, are not evidence."⁶

To the contrary, each of the Examiner's statements regarding the ordinary artisan's motivation to select and combine references are conclusory and unsupported. The Examiner has provided no support in the form of prior art reference, affidavit, declaration, or concrete evidence other than in the form of an argument, teaching that the artisan of ordinary skill would have been motivated to select and combine all, some or even one of the previously cited references (i.e Berger et al. or Akitaya et al.) with Chatterjee et al. as the Examiner speculates. This is because the only source guiding the Examiner to pair Chatterjee et al. in combination with Berger et al. or Akitaya et al. as cited in the 2/4/2003 Office Action is the present invention, that is, through the hindsight of one in possession of the present disclosure.

CONCLUSION

All grounds of rejection of the Office Action of February 4, 2002 have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that Applicant's claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

⁵*In re Dembiczak*, 175 F.3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999), citing *C.R. Bard*, 157 F.3d 1340 at 1352, 48 USPQ2d at 1232.

⁶*In re Dembiczak*, 175 F.3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999), citing *McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed. Cir. 1993).

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